Thiiranation of 2′-Adamantylidene-9-benzonorbornenylidene and *cis*- and *trans*-Cyclooctenes with 4,4′-Dithiodimorpholine in Acetic Anhydride

Yoshiaki Sugihara,* Hiroki Koyama, Yuri Yasukawa, and Juzo Nakayama*
Department of Chemistry, Graduate School of Science and Engineering, Saitama University,
Sakura-ku, Saitama 338-8570

(Received September 8, 2008; CL-080851; E-mail: ysugi@chem.saitama-u.ac.jp)

Thiiranation of 2′-adamantylidene-9-benzonorbornenylidene (**1**) with 4,4′-dithiodimorpholine (**5**) in Ac_2O at −15 °C gave thiiranes **2** and **3** without the decomposition of the thermodynamically less stable **3**. *cis*- and *trans*-Cyclooctenes underwent thiiranation with retention of their stereochemistry.

The introduction of sulfur-containing functionalities in organic compounds plays an important role in syntheses of useful materials,[1,2] because these functionalities induce a remarkable character change in the compound.[3] While thiiranation of alkenes, which is an important sulfuration method for introducing one sulfur atom onto a C=C bond, has been investigated,[1] a few reports have dealt with the general methods.[4] Most thiiranation methods have problems such as difficulty in analyzing the reaction mixture and synthesizing the thiiranation reagent, a lack of generality when using alkenes, and decomposition of the resulting thiiranes to other compounds under the thiiranation conditions. In our on-going study on synthesis and sulfuration of alkenes,[5] we have designed a novel alkene to overcome these problems, and synthesized 2′-adamantylidene-9-benzonorbornenylidene (**1**), which is a model alkene suitable for investigating the thiiranation conditions (Figure 1).[6] Sulfuration of **1** with S_8 gave a mixture of thiiranes **2** and **3** along with the recovery of **1**, while that with S_XCl_2 afforded **2**, **3**, and **4**. The thiirane **3** decomposed to **1** and **2** with elemental sulfur, and to **2** and **4** with S_XCl_2 under the sulfuration conditions. Recently, we revealed that 4,4′-dithiodimorpholine (**5**), which is a commercially available vulcanizing agent, and 4,4′-tetrathiodimorpholine (**6**) activated by Brønsted acids, such as carboxylic and sulfonic acids, were able to sulfurate **1** to form **2** and **3** at room temperature.[7] Since the reaction was sluggish and the decomposition of **3** to **1** and **2** proceeded, the method seemed unsuitable for the thiiranation of alkenes. However, if **5** is activated with other reagents efficiently, thiiranation with **5** would be more useful. We report here the thiiranation of **1** with **5** and acid anhydride, the decomposition of **3** under thiiranation conditions, and the thiiranation of other alkenes.

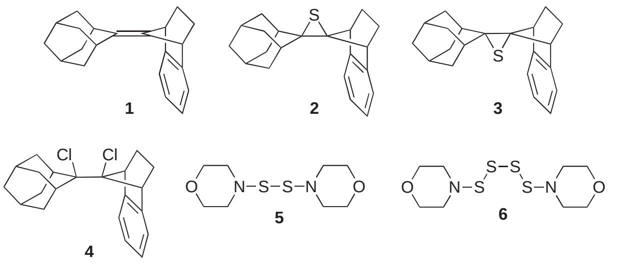


Figure 1.

Table 1. Screening of acid anhydride for thiiranation of **1** with **5**

$$1 \xrightarrow[\text{acid anhydride}]{5} 2 + 3$$

Entry	Acid anhydride (molar equiv)	**5**/mol equiv	Conditions	Yield/%[b]		
				2	**3**	**1**
1	Tf_2O (1.0)	1.0	CH_2Cl_2, −30 °C, 6 h	94	—	—
2	AcOTf (1.0)	1.0	CH_2Cl_2, −30 °C, 9 h	76	8	—
3	$(CF_3CO)_2O$ (1.0)	1.0	CH_2Cl_2, −30 °C, 24 h	75	8	4
4	Ts_2O (1.0)	1.0	CH_2Cl_2, rt, 65 h	18[c]	26[c]	56[c]
5	Ac_2O (1.0)	1.0	CH_2Cl_2, rt, 45 h	—	3	92
6	Ac_2O (excess)[a]	1.0	−15 °C, 40 h	14[c]	84[c]	2[c]
7	Ac_2O (excess)[a]	0.5	−15 °C, 60 h	15	52	22

[a] Ac_2O was used as solvent. [b] Isolated yield. [c] Determined by ¹H NMR.

A combination of **5** and acid anhydride was used for successful thiiranation of **1** (Table 1). Thus, **1** reacted with 1.0 molar equiv of **5** and 1.0 molar equiv of Tf_2O, AcOTf, or $(CF_3CO)_2O$ in CH_2Cl_2 even at −30 °C to afford the thiiranes in good yields (Entries 1–3). Both the thiiranation rate and the ratio of **2** to **3** seem to decrease as the reactivity of acid anhydride to a nucleophilic reagent decreases. The thiiranation with Ts_2O was more sluggish than with Tf_2O, AcOTf, and $(CF_3CO)_2O$ (Entry 4). The thiiranation with 1.0 molar equiv of Ac_2O, however, proceeded to form **3** in a very small quantity (Entry 5). Surprisingly, when **1** reacted with **5** in Ac_2O, the thiiranation occurred even at −15 °C to give **2** and **3** in 14% and 84% yields, respectively (Entry 6). On the other hand, when 0.5 molar equiv of **5** was used, the thiiranation gave **2** and **3** in 15% and 52% yields, respectively, along with the recovery of **1** in 22% yield, suggesting that one or more sulfur atoms of **5** were introduced into **1** in the thiiranation (Entry 7).

The thiirane **3** is thermodynamically less stable than **2** by 13.4 kJ mol⁻¹;[6] thus, the reactions of **3**, which are accompanied by C–S bond cleavage, tend to produce **2** together with **1**.[7] Therefore, the decomposition of **3** was investigated to determine

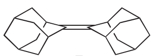
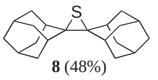
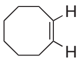
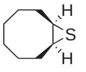
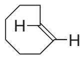
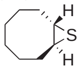
Table 2. Decomposition of **3** to **1** and **2** under the thiiranation conditions

$$3 \xrightarrow[\text{acid anhydride}]{\mathbf{5}\ \text{(1.0 molar equiv)}} 1 + 2$$

Entry	Acid anhydride (molar equiv)	Conditions	Yield/%[b]		
			1	**2**	**3**
1	Tf_2O (1.0)	CH_2Cl_2, −30 °C, 6 h	—	quant.	—
2	AcOTf (1.0)	CH_2Cl_2, −30 °C, 9 h	—	94[c]	—
3	$(CF_3CO)_2O$ (1.0)	CH_2Cl_2, −30 °C, 24 h	2	86	12
4	Ts_2O (1.0)	CH_2Cl_2, rt, 65 h	24	26	50
5	Ac_2O (1.0)	CH_2Cl_2, rt, 45 h	—	—	quant.
6	Ac_2O (excess)[a]	−15 °C, 40 h	—	—	quant.
7	Ac_2O (excess)[a]	−15 °C, 144 h	—	—	95[c]
8	Ac_2O (excess)[a]	rt, 42 h	10	41	49

[a] Ac_2O was used as solvent. [b] Determined by ¹H NMR. [c] Isolated yield.

Table 3. Thiiranation of alkene with **5** in Ac_2O at $-15\,°C$

Alkene	Reaction time	Product (yield)[a]
 **7**	4 d	 **8** (48%) + **7** (50%)
 **9**	7 d	 **11** (9%) + **9** (22%)
 **10**	2 d	 **12** (63%)[b]

[a]Isolated yield. [b]A small amount of **9** and **10** was observed.

suitable thiiranation conditions (Table 2). The thiirane **3** decomposed with **5** and Tf_2O or AcOTf to give a high yield of **2** (Entries 1 and 2). As $(CF_3CO)_2O$ or Ts_2O was employed, the decomposition proceeded, but the recovery of **3** was observed (Entries 3 and 4). The decomposition with 1.0 molar equiv of Ac_2O at room temperature did not occur (Entry 5). However, **3** did not decompose in Ac_2O at $-15\,°C$, indicating that the aforementioned thiiranation of **1** in Ac_2O at $-15\,°C$ proceeded without the decomposition of **3** (Entries 6 and 7). A rise in the temperature of the reaction in Ac_2O to room temperature resulted in the decomposition of **3** (Entry 8).

Considering these results, the thiiranation performed in Ac_2O at $-15\,°C$ would provide the best results. Therefore, the thiiranation of other alkenes was performed under these conditions (Table 3).[8] 2,2′-Biadamantylidene (**7**) reacted with **5** to form the corresponding thiirane **8**. *cis*- and *trans*-Cyclooctenes (**9** and **10**) also underwent thiiranation by this method. Thus, **9** reacted with **5** under similar conditions to yield *cis*-sulfide **11**[9,10a] and the recovery of **9** in 9% and 22% yields, respectively. The thiiranation of **10**, which gave *trans*-sulfide **12**[9,10b] in 63% yield, proceeded faster than that of **9** because of a difference of their reactivity. In this reaction, small amounts of **10** and **9** were detected in the reaction mixture by ^1H NMR. These results indicate that this thiiranation proceeds with retention of the configuration of the starting alkene to yield the corresponding thiirane. When the thiiranation of **9** was performed at 40 °C for 2 days, an oily complex mixture containing no thiirane was obtained.

The thiiranation of **13**–**16** in Ac_2O at $-15\,°C$ resulted in the quantitative recovery of the starting alkenes (Figure 2). These alkenes seemed to be less reactive than the aforementioned alkenes. When the reaction temperature was elevated to 60 °C, the reaction of **13** afforded **13** and **14** in 18% and 73% yields, respectively, although the reaction of **14** resulted in the recovery of **14**. Both reactions at 60 °C also produced elemental sulfur. On the other hand, an oily mixture, which contained unidentified compounds, was obtained in each thiiranation of **15** at room temperature and that of **16** at 40 °C.

A possible mechanism of the sulfuration is as follows (Scheme 1). Compound **5** reacts with Ac_2O to form **17**. Then, **17** undergoes a substitution reaction at its sulfur atom with **5** to afford **19** and **18**, which acts as a thiiranation reagent similar to **17**. Alkene reacts with **17** or **18** to form **20**, which then undergoes nucleophilic substitution at the sulfur atom next to the positively charged sulfur atom to extrude the thiirane. The compound **22**, which acts as a thiiranation reagent, was also formed in the substitution. The decomposition of the resulting thiirane proceeds through **20** formed by the reaction of the thiirane with **17** or **18**, and ring-opened carbenium ion **21**. The isomerization of **13** to **14** also occurs through **20** and **21**.[5d,6,11]

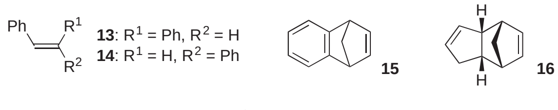
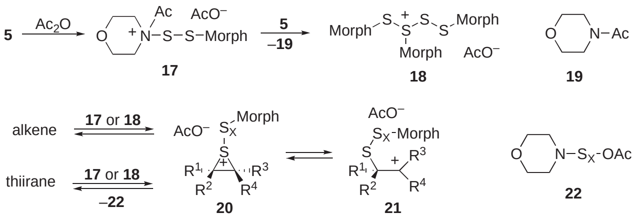


Figure 2.



Scheme 1.

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References and Notes

1 W. Adam, R. M. Bargon, *Chem. Rev.* **2004**, *104*, 251.
2 M. G. Voronkov, N. S. Vyazankin, E. N. Deryagina, A. S. Nakhmanovich, V. A. Usov, *Reactions of Sulfur with Organic Compounds*, Consultants Bureau, NewYork, **1987**; J. P. Donahue, *Chem. Rev.* **2006**, *106*, 4747; T. Kondo, T. Mitsudo, *Chem. Rev.* **2000**, *100*, 3205.
3 E. Block, *Reactions of Organosulfur Compounds*, Academic, New York, **1973**; S. Oae, *Organic Sulfur Chemistry: Structure and Mechanism*, CRC, Florida, **1991**; P. Metzner, A. Thuillier, *Sulfur Reagents in Organic Synthesis*, Academic, London, **1993**; R. J. Cremlyn, *An Introduction to Organosulfur Chemistry*, John Wilcy & Sons, Chichester, **1996**.
4 W. Adam, S. Weinkötz, *Chem. Commun.* **1996**, 177; W. Adam, S. Weinkötz, *J. Am. Chem. Soc.* **1998**, *120*, 4861; W. Adam, R. M. Bargon, W. A. Schenk, *J. Am. Chem. Soc.* **2003**, *125*, 3871.
5 a) J. Nakayama, Y. Ito, A. Mizumura, *Sulfur Lett.* **1992**, *14*, 247. b) Y. Sugihara, H. Takeda, J. Nakayama, *Tetrahedron Lett.* **1998**, *39*, 2605. c) Y. Sugihara, H. Takeda, J. Nakayama, *Eur. J. Org. Chem.* **1999**, 597. d) Y. Sugihara, K. Noda, J. Nakayama, *Bull. Chem. Soc. Jpn.* **2000**, *73*, 2351. e) Y. Sugihara, K. Noda, J. Nakayama, *Tetrahedron Lett.* **2000**, *41*, 8907. f) K. Noda, Y. Sugihara, J. Nakayama, *Heteroat. Chem.* **2001**, *12*, 625.
6 Y. Sugihara, A. Kobiki, J. Nakayama, *Heterocycles*, in press.
7 Y. Sugihara, H. Nozumi, J. Nakayama, submited for publication.
8 Typical experimental procedures for the thiiranation of alkenes are as follows. To a stirred solution of alkene (1.0 mmol) in Ac_2O (3.0 mL) at $-15\,°C$ under argon atmosphere, **5** (1.0 molar equiv) was added. After stirring at $-15\,°C$, the reaction mixture was added gradually to a cold aqueous LiOH solution. After the mixture was diluted with Et_2O, the organic layer was separated, washed with H_2O, dried over $MgSO_4$, and evaporated. The crude product was purified by silica-gel column chromatography to afford the corresponding thiirane.
9 A. Ishii, M. Suzuki, R. Yamashita, *Tetrahedron* **2006**, *62*, 5441.
10 a) W. Adam, R. M. Bargon, *Chem. Commun.* **2001**, 1910. b) W. Adam, R. M. Bargon, *Eur. J. Org. Chem.* **2001**, 1959.
11 Y. Sugihara, Y. Aoyama, J. Nakayama, *Chem. Lett.* **2001**, 980.

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